

University of Groningen

Long term treatment related upper limb morbidity and quality of life after sentinel lymph node biopsy for stage I or II breast cancer

Rietman, J.S.; Geertzen, J.H.B.; Hoekstra, H.J.; Baas, P.; Dolsma, W.V.; de Vries, J; Groothoff, J.W.; Eisma, W.H.; Dijkstra, P.U.

Published in:
EJSO

DOI:
[10.1016/j.ejso.2005.11.008](https://doi.org/10.1016/j.ejso.2005.11.008)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Rietman, J. S., Geertzen, J. H. B., Hoekstra, H. J., Baas, P., Dolsma, W. V., de Vries, J., Groothoff, J. W., Eisma, W. H., & Dijkstra, P. U. (2006). Long term treatment related upper limb morbidity and quality of life after sentinel lymph node biopsy for stage I or II breast cancer. *EJSO*, 32(2), 148-152.
<https://doi.org/10.1016/j.ejso.2005.11.008>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Long term treatment related upper limb morbidity and quality of life after sentinel lymph node biopsy for stage I or II breast cancer

J.S. Rietman^{a,b,c,*}, J.H.B. Geertzen^{b,c}, H.J. Hoekstra^d, P. Baas^e, W.V. Dolsma^f, J. de Vries^d, J.W. Groothoff^c, W.H. Eisma^{b,c}, P.U. Dijkstra^{b,c}

^aDepartment of Rehabilitation Medicine, Martini Hospital, P.O. Box 30033, 9700 RM Groningen, The Netherlands

^bDepartment of Rehabilitation Medicine, Groningen University Hospital, Groningen, The Netherlands

^cNorthern Centre for Health Care Research, University Groningen, Groningen, The Netherlands

^dDepartment of Surgical Oncology, Groningen University Hospital, Groningen, The Netherlands

^eDepartment of Surgery, Martini Hospital, Groningen, The Netherlands

^fDepartment of Radiation Oncology, Groningen University Hospital, Groningen, The Netherlands

Accepted 21 November 2005

Available online 4 January 2006

Abstract

Background: In a prospective study, long term upper-limb morbidity, perceived disabilities in activities of daily life (ADL) and quality of life (QOL) were assessed before and 2 years after sentinel lymph node biopsy (SLNB) or axillary lymph node dissections (ALND) for breast cancer.

Methods: Two hundred and four patients with stage I/II breast cancer, mean age 55.6 years (SD: 11.6) entered the study and 181 patients (89%) could be evaluated after 2 years. Fifty-seven patients underwent SLNB (31%) and 124 patients underwent an ALND (69%). Assessments included pain, shoulder range of motion, muscle strength, arm volume, perceived shoulder disability in ADL and QOL.

Results: Significant ($P < 0.05$) changes between before and 2 years after surgery were found in almost all assessments of shoulder function, ADL and several QOL subscales. Patients in the ALND group showed significant more changes in range of motion (ROM), grip strength, arm volume, ADL and QOL physical- and role functioning, pain and sleeplessness and arm symptoms compared to the SLNB group. Multivariate linear regression analysis showed that ALND could predict decrease of ROM, grip strength, ADL and physical functioning (QOL) and increase of arm volume, pain and arm symptoms score (QOL). Radiation on the axilla predicts an additional decrease in shoulder ROM and increase of arm volume.

Conclusion: Two years after surgery for breast cancer, patients show significantly less treatment related upper limb morbidity, perceived disability in ADL and worsening of QOL after SLNB compared with ALND.

© 2005 Elsevier Ltd. All rights reserved.

Keywords: Breast cancer; Sentinel lymph node; Radiation; Morbidity; Quality of life

Introduction

The aim of modern breast cancer treatment is to obtain local tumour control, optimal lymph node staging with minimal treatment related morbidity and when possible preservation of the breast. Due to breast cancer screening programs and multimodality breast cancer treatment the

number of patients cured after breast cancer is still increasing as do the 5 and 10 year survival.^{1,2}

Axillary lymph node status is an important prognostic factor in patients with breast cancer.^{3–5} Axillary lymph node dissection (ALND) still is associated with upper limb morbidity.⁶ The impact of upper limb morbidity on disabilities in ADL and QOL in breast cancer patients has rarely been studied with modern assessment instruments.^{6–8} Sentinel lymph node biopsy (SLNB) was introduced for staging of the axilla to reduce the number of unnecessary ALND's.⁹ SLNB is an accurate and safe procedure to predict metastatic disease in clinically negative axillary lymph nodes.^{9–11} An increasing number of studies reported

* Corresponding author. Address: Department of Rehabilitation Medicine, Martini Hospital Groningen, P.O. Box 30033, NL-9700 RM Groningen, The Netherlands. Tel.: +31 50 5245885/5245886; fax: +31 50 5245183.

E-mail address: j.s.rietman@planet.nl (J.S. Rietman).

less treatment related morbidity for SLNB in comparison to ALND.^{12–20} Generally disability in ADL of the SLNB group was less than that of the ALND group.^{13,16,19} A shortcoming in most studies is the absence of pre-treatment assessment and the absence of reliable and validated assessment instruments. Although association between upper limb morbidity and poorer QOL was described, QOL is seldom considered in the debate on axillary surgery.^{6,8,20–22}

The aim of the current prospective study was to analyse long-term upper limb morbidity, perceived disability in ADL and QOL 2 years after SLNB or ALND. The second aim was to analyse to which extent ALND and other treatment variables could predict upper limb morbidity, perceived disability and decreased QOL.

Patients and methods

From June 1999 to June 2001, patients with breast carcinoma stage I or stage II entered the study.²³ Patients were retrieved from the Groningen University Medical Centre and the Martini Hospital Groningen. Informed consent was obtained from the participating patients. The protocol was approved by the Institutional Review Board of both hospitals. Two groups of breast cancer patients participated in the prospective study, patients who underwent conventional breast cancer treatment with an ALND and patients who were treated according to the SLNB concept. Sentinel lymph nodes were identified by pre-operative lymphoscintigraphy followed by intraoperative tracing using a gamma probe and Patent blue dye[®] (Blue Patenté; Labatoire Guerbet, Aulnay-sous-Bois, France). The procedure has been previously described in detail.²⁴ If pathological examination revealed metastases in the sentinel lymph node, ALND was performed within two weeks after SLNB.

Pain (VAS²⁵), upper limb function (range of motion, muscle strength, arm volume),^{26–31} numbness, ADL^{32–34} and QOL^{35,36} were assessed 1 day before surgery (t0) and 2 years after surgery (t1) (Table 1). The shoulder disability questionnaire (SDQ) was designed to evaluate the ability to perform daily activities in patients with shoulder disorders.^{32,37,38} The Groningen activity restriction scale (GARS) assesses the perceived restrictions (disability) in performing 18 ADLs.^{33,34} A higher score represents more functional status limitation.

Quality of life was assessed with help of the EORTC QLQ-C30 questionnaire supplemented with the EORTC breast module (EORTC QLQ-BR23).^{35,36}

Statistical analyses included descriptive statistics and *t*-tests for independent samples for between-group comparisons and *t*-tests for dependent samples for within-group comparisons. Pearson's chi-squared test was used for dichotomous variables. To answer the question in which extent treatment variables could predict upper limb morbidity, perceived disability and poorer QOL,

Table 1

Upper limb morbidity and disability 2 years after breast cancer treatment (*n* = 181)

| | Before surgery (mean ± SD) | Change (mean ± SD) | <i>P</i> value |
|------------------------------------|-------------------------------|--------------------|----------------|
| Pain (VAS: 0–10) | 0.4 ± 1.1 | 0.3 ± 1.7 | 0.01 |
| Numbness (<i>n</i>) ^a | 0 (0%) | 114 | <0.001 |
| Forward flexion (°) | 172.4 ± 11.9 | −4.4 ± 12.6 | <0.001 |
| Abduction (°) | 168.0 ± 22.6 | −16.2 ± 31.0 | <0.001 |
| Abduction/external rotation (°) | 87.1 ± 6.6 | −6.0 ± 12.3 | <0.001 |
| External rotation (°) | 67.7 ± 13.0 | −5.9 ± 13.6 | <0.001 |
| Strength shoulder abductors (Nm) | 151.0 ± 36.8 | −10.0 ± 29.9 | <0.001 |
| Strength elbow flexors (Nm) | 180.0 ± 40.7 | 5.8 ± 40.5 | 0.057 |
| Grip strength (Nm) | 297.8 ± 64.0 | −33.6 ± 51.7 | <0.001 |
| Volume arm (ml) | 2162 ± 414 | 124 ± 241 | <0.001 |
| SDQ (0–100) | 8.2 ± 19.7 | 10.5 ± 29.9 | <0.001 |
| GARS (18–72) | 19.6 ± 3.7 | 1.8 ± 5.7 | <0.001 |

(°), grades; Nm, Newton meter; ml, millilitre; SD, standard deviation; SDQ, the shoulder disability questionnaire³²; GARS, the Groningen activity restriction scale.^{33,34}

^a No standard deviations were given because it concerns a dichotomous variable.

multivariate linear regression analyses were performed. Differences were accepted as significant if *P* values were < 0.05. SPSS[®] Base 11.5 software for Windows[®], SPSS Inc., was used for statistical analysis.

Results

In the period 1999–2001, 204 consecutive patients with invasive breast carcinoma were included in the study. Two years after surgery 23 of the 204 patients (11%) could not be assessed. Fourteen patients belonged to the ALND group; six patients died of metastatic disease; one patient had a breast reconstruction and was excluded from assessment, seven patients withdrew from the study because of other reasons. Nine patients belonged to the SLNB group; one patient had distant metastasis, one patient refused further treatment and seven of them found the assessment protocol bothersome and chose to withdraw from the study.

One hundred and eighty-one patients could be evaluated after 2 years; 57 patients (32%) in the SLNB group and 124 patients (68%) in the ALND group. TNM classification, receptor status and treatment characteristics of these patients are presented in an earlier study.³⁸

Substantial long-term treatment-related upper-limb morbidity and increasing of disability was observed for the whole study group (Table 1). Also significant changes were found for QOL assessed with the EORTC QLQ-C30/QLQ-BR23 (Table 2).

Several changes in upper-limb function (upper-limb morbidity), ADL (perceived disability) and QOL between before surgery and 2 years after treatment were significantly

Table 2

QOL (EORTC QLQ C-30 and QLQ-BR23) 2 years after breast cancer treatment ($n=181$)

| | Before surgery (mean \pm SD) | Change (mean \pm SD) | <i>P</i> value |
|--|-----------------------------------|---------------------------|----------------|
| Functional scales | | | |
| Physical functioning | 91.3 \pm 11.1 | −5.2 \pm 13.3 | <0.001 |
| Role functioning | 92.4 \pm 16.2 | −5.4 \pm 23.8 | 0.003 |
| Emotional functioning | 71.2 \pm 19.9 | 15.8 \pm 20.7 | <0.001 |
| Cognitive functioning | 87.4 \pm 15.5 | −1.1 \pm 30.5 | 0.624 |
| Social functioning | 92.3 \pm 14.9 | 0 \pm 18.8 | 1.000 |
| General health score QOL | 80.4 \pm 18.0 | −1.2 \pm 19.8 | 0.411 |
| Symptom scales/items | | | |
| Fatigue scale | 16.4 \pm 20.2 | 4.2 \pm 17.5 | 0.002 |
| Nausea and vomiting scale | 3.0 \pm 11.1 | 1.7 \pm 16.1 | 0.166 |
| Pain scale | 8.8 \pm 17.5 | 6.1 \pm 21.4 | <0.001 |
| Dyspnoea | 5.8 \pm 15.4 | 3.7 \pm 18.4 | 0.007 |
| Insomnia (sleeplessness) | 23.7 \pm 27.3 | −4.1 \pm 29.4 | 0.063 |
| Appetite loss | 7.5 \pm 16.4 | −2.1 \pm 20.1 | 0.173 |
| Constipation | 2.6 \pm 11.9 | 2.4 \pm 15.4 | 0.037 |
| Diarrhea | 4.1 \pm 12.1 | −1.5 \pm 12.6 | 0.117 |
| Financial difficulties | 1.7 \pm 7.3 | 4.2 \pm 20.5 | 0.006 |
| QLQ-BR23 (breast cancer module) | | | |
| Side-effects | 8.0 \pm 8.4 | 4.8 \pm 13.2 | <0.001 |
| Hair loss (only three patients) | 22.2 \pm 38.5 | 22.2 \pm 38.5 | 0.423 |
| Body image | 94.7 \pm 10.6 | −3.2 \pm 17.1 | 0.014 |
| Future perspective | 59.7 \pm 25.1 | 12.7 \pm 28.2 | <0.001 |
| Sexual functioning ($n=137$) | 22.6 \pm 20.1 | 1.2 \pm 19.3 | 0.496 |
| Sexual satisfaction ($n=57$) | 56.8 \pm 22.1 | −4.9 \pm 27.0 | 0.185 |
| Arm symptoms | 4.9 \pm 10.2 | 8.8 \pm 19.4 | <0.001 |
| Breast symptoms | 10.9 \pm 14.2 | 1.3 \pm 18.1 | 0.334 |

EORTC QLQ, European organization on research and treatment of cancer quality of life questionnaire.³⁵

different between the SLNB group and the ALND group in favour of the first (Table 3).

Multivariate linear regression analysis to predict the mean change in upper-limb function, ADL and QOL between before treatment and 2 years after treatment for independent variables: age, axillary surgery, breast surgery, radiation breast, radiation axilla and chemotherapy was performed. ALND was a significant factor in the prediction in the majority of mean changes in the performed assessments of upper-limb function (abduction, grip strength, arm volume), ADL (SDQ, GARS) and QOL (physical functioning, pain, sleeplessness, diarrhea, arm symptoms). Radiation of the axilla was significant in four analyses: forward flexion, abduction, abduction/external rotation and arm volume. Mastectomy was significant associated with a lower body image (details not shown).

Discussion

Significant treatment related upper limb morbidity, associated ADL disabilities and decreased QOL exist 2 years after SLNB or ALND. Treatment related upper limb morbidity, perceived disabilities in ADL and worsening of QOL 2 years after surgery is significantly less after SLNB compared to ALND. In the assessment of changes in upper

Table 3

Change of upper limb function, disability and QOL in the SLNB group and the ALND group between before surgery and 2 years after surgery

| Variable | SLNB ($n=57$) (t1–t0) Mean change \pm SD | ALND ($n=124$) (t1–t0) Mean change \pm SD | Differences in mean change ALND–SLNB | |
|--|---|---|---|----------------|
| | | | Mean difference | <i>P</i> value |
| Numbness (n^a) | 10 (18%) | 104 (84%)* | 94 | <0.001 |
| Abduction (°) | −5.5 \pm 21.0 | −21.0 \pm 33.5* | 15.5 | <0.001 |
| Abduction/external rotation (°) | −3.5 \pm 8.0* | −7.2 \pm 13.7* | 3.7 | 0.025 |
| Grip strength (Nm) | −17.2 \pm 48.2* | −41.3 \pm 51.7* | 24.1 | 0.004 |
| Volume arm (ml) | −2 \pm 142.5 | 182 \pm 255.6* | 184 | <0.0001 |
| GARS (18–72) | 0.2 \pm 3.5 | 2.5 \pm 6.3* | 2.3 | 0.002 |
| EORTC QLQ C30 | | | | |
| Physical functioning | −0.9 \pm 10.6 | −7.3 \pm 13.9* | 6.4 | 0.001 |
| Role functioning | −0.3 \pm 21.7 | −7.8 \pm 24.4* | 7.5 | 0.041 |
| Pain | 0.6 \pm 18.4 | 8.7 \pm 22.4* | 8.1 | 0.012 |
| Insomnia (sleeplessness) | −11.3 \pm 27.9* | −0.8 \pm 29.6 | 10.5 | 0.027 |
| QLQ-BR23 (breast cancer module) | | | | |
| Arm symptoms | 3.0 \pm 11.5 | 11.5 \pm 21.7* | 8.5 | 0.001 |

Results of *t*-test for independent samples. Nm, Newton meter; cm, centimetre; (°), degree; *, significant changes between before and after surgery ($P<.05$). GARS, the Groningen activity restriction scale.^{33,34} EORTC QLQ, European organization on research and treatment of cancer quality of life questionnaire.³⁵

^a No standard deviations were given because it concerns a dichotomous variable.

limb function, ADL and QOL, ALND is the most frequent found predictor of deterioration. Additional radiation on the axilla predicts a further decrease in shoulder ROM and arm oedema.

This outcome confirms results of previous studies suggesting that SLNB is associated with less treatment related upper-limb morbidity although these are no long-term comparative studies.^{12–19,21,37,38} This is the first prospective study comparing SLNB and ALND with pre- and long-term post-surgical assessments of upper limb function, ADL and QOL. In a recent systematic review and two previous studies we emphasized the importance of the baseline assessment and the use of reliable and validated assessment instruments.^{6,37,38}

The perceived disabilities in ADL assessed in this study with the SDQ and GARS were significant but relatively mild. Concerning QOL for the whole study group a significant decrease was found over the 2 years for physical and role functioning and body image whereas emotional functioning and future perspective showed significant increase over this period (Table 2). The improvement of emotional functioning and future perspective can be explained by the fact that the first assessment took place 1 day before surgery. Obviously at this time patients were nervous and stressed and also uncertain about their future perspective.²¹ Two years later these aspects were highly improved.

Some scores on symptom scales increased significantly such as fatigue, pain, dyspnoea, constipation, side-effects of

systemic therapies and arm problems (Table 2). These outcomes correspond with results found in earlier studies done on breast cancer treatment and QOL.^{6–8,21} Comparing SLNB and ALNB significantly differences in mean change over the 2 years were found for physical and role functioning and also for symptom items such as pain, insomnia (sleeplessness) and arm symptoms in favour for the SLNB group (Table 3).

The interpretation of the scores on the EORTC QLQ-C30 and QLQ-BR23 in relation to clinical relevance needs some discussion. King did a review on the interpretation of scores from the EORTC QLQ-C30 and stated that the smallest clinically important difference may vary with clinical context.⁴¹ All the statistically significant differences found in our study within and between the groups could be interpreted as relatively small clinically important differences except the improvement of emotional functioning which could be interpreted as a very large clinically important difference.⁴¹

Multivariate linear regression analysis to predict mean change in upper-limb function, ADL and QOL between before and 2 years after surgery showed that radiation on the axilla is a significant factor in the prediction of impaired ROM and increase of arm volume. This finding is a conformation of results of some other studies and may be explained by radiation induced subcutaneous fibrosis affecting the ROM and lymph drainage.^{6,8,42,43} ALND as predictor of upper limb morbidity was observed for abduction, grip strength, arm volume, ADL and some scales of the QLQ-C30 and QLQ-BR23. This result confirms results of other studies in which the extent of axillary treatment was found to be related to late morbidity.^{6,19,20,42} Although the comparison between mastectomy and breast conserving surgery was not subject of this study we found that mastectomy predicts a part of the decrease in body image. A lower body image in mastectomy patients was earlier described.⁴⁴

Acknowledgements

The authors like to thank J. Kootstra for her assistance by the logistics and assessments in this study.

References

1. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, et al. Cancer statistics, 2004. *CA Cancer J Clin* 2004;**54**(1):8–29.
2. Levi F, Lucchini F, Negri E, La Vecchia C. The decline in cancer mortality in the European Union, 1988–1996. *Eur J Cancer* 2000;**36**: 1965–8.
3. Donegan WL. Prognostic factors: stage and receptor status in breast cancer. *Cancer* 1992;**70**:1755–64.
4. Carter CL, Allen C, Henson DE. Relation of tumour size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer* 1989;**63**: 181–7.
5. Schaapveld M, Otter R, de Vries EG, Fidler V, Grond JA, van der Graaf WT, et al. Variability in axillary lymph node dissection for breast cancer. *J Surg Oncol* 2004;**87**(1):4–12.
6. Rietman JS, Dijkstra PU, Hoekstra HJ, Eisma WH, Szabo BG, Groothoff JW, et al. Late morbidity after treatment of breast cancer in relation to daily activities and quality of life; a systematic review. *Eur J Surg Oncol* 2003;**29**(3):229–38.
7. Poole K, Fallowfield LJ. The psychological impact of post-operative arm morbidity following axillary surgery for breast cancer: a critical review. *The Breast* 2002;**11**:81–7.
8. Rietman JS, Dijkstra PU, Debreczeni R, Geertzen JHB, Robinson DPH, Vries de J. Impairments, disabilities and health related quality of life after treatment for breast cancer: a follow-up study 2.7 years after surgery. *Disabil Rehabil* 2004;**26**(2):78–84.
9. Giuliano AE, Dale PS, Turner RR, Morton DL, Evans SW, Krasne DL, et al. Improved axillary staging of breast cancer with sentinel lymphadenectomy. *Ann Surg* 1995;**222**(3):394–9.
10. Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymphnodes. *Lancet* 1997;**349**(9069):1864–7.
11. Naik AM, Fey J, Gemignani M, Heerdt A, Montgomery L, Petrek J, et al. The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection: a follow-up study of 4008 procedures. *Ann Surg* 2004;**240**(3):462–71.
12. Schrenk P, Rieger R, Shamiyeh A, Wayand W. Morbidity following sentinel lymph node biopsy versus axillary lymph node dissection for patients with breast carcinoma. *Cancer* 2000;**88**:608–14.
13. Haid A, Köberle-Wührer R, Knauer M, Burtscher J, Fritzsche H, Peschina W, et al. Morbidity of breast cancer patients following complete axillary dissection or sentinel node biopsy only: a comparative evaluation. *Br Cancer Res Treat* 2002;**73**:31–6.
14. Burak WE, Hollenbeck ST, Zervos EE, Hock KL, Kemp LC, Young DC. Sentinel lymph node biopsy results in less postoperative morbidity compared with axillary lymph node dissection for breast cancer. *Am J Surg* 2002;**183**(1):23–7.
15. Temple LKF, Baron R, Cody HS, Fey JV, Thaler HT, Borgen PI, et al. Sensory morbidity after sentinel lymph node biopsy and axillary dissection: a prospective study of 233 women. *Ann Surg Oncol* 2002;**9**(7):654–62.
16. Swenson KK, Nissen MJ, Cernovsky C, Swenson L, Lee MW, Tuttle TM. Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. *Ann Surg Oncol* 2002;**9**(8):745–53.
17. Haid A, Kuehn P, Konstantiniuk R, Köberle-Wührer R, Knauer M, Kreienberg R, et al. Shoulder-arm morbidity following axillary dissection and sentinel node only biopsy for breast cancer. *Eur J Surg Oncol* 2002;**28**:705–10.
18. Leidenius M, Leppänen E, Krogerus L, von Smitten K. Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer. *Am J Surg* 2003;**185**:127–30.
19. Schijven MP, Vingerhoets AJJM, Rutten HJT, Nieuwenhuijzen GAP, Roumen RMH, van Bussel ME, et al. Comparison of morbidity between axillary lymph node dissection and sentinel node biopsy. *Eur J Surg Oncol* 2003;**29**:341–50.
20. Ververs JMMA, Roumen RMH, Vingerhoets AJJM, Vreugdenhil G, Coebergh JWW, Crommelin MA, et al. Risk, severity and predictors of physical and psychological morbidity after axillary lymph node dissection for breast cancer. *Eur J Cancer* 2001;**37**:991–9.
21. Peintinger F, Reitsamer R, Stranzl H, Ralph G. Comparison of quality of life and arm complaints after axillary lymph node dissection vs sentinel lymph node biopsy in breast cancer patients. *Br J Cancer* 2003;**89**:648–52.
22. Engel J, Kerr J, Schlesinger-Raab A, Sauer H, Hölzel D. Axilla surgery severely affects quality of life: results of a 5-year prospective study in breast cancer patients. *Br Cancer Res Treat* 2003;**79**:47–57.

23. International Union Against Cancer. Breast tumors. In: Sobin LH, Wittekind Ch, editors. *TNM classification of malignant tumors*. 6th ed. New York: Wiley-Liss; 2002. p. 131–42.
24. Rutgers EJ, Jansen L, Nieweg OE, de Vries J, Schraffordt Koops H, Kroon BB. Technique of sentinel node biopsy in breast cancer. *Eur J Surg Oncol* 1998;**24**(4):316–9.
25. Gerber L, Lampert M, Wood C, Duncan M, D'Angelo T, Schain W, et al. Comparison of pain, motion and edema after modified radical mastectomy vs. local excision with axillary dissection and radiation. *Br Cancer Res Treat* 1992;**21**(2):139–45.
26. Green S, Buchbinder R, Forbes A, Bellamy N. A standardised protocol for measurement of range of movement of the shoulder using the Plurimeter-V inclinometer and assessment of its intrarater and interrater reliability. *Arthritis Care Res* 1998;**11**(1):43–52.
27. van der Ploeg RJO. Hand-held dynamometry. Thesis. The Netherlands: University of Groningen; 1992.
28. van der Ploeg RJO, Fidler V, Oosterhuis HJGH. Hand-held myometry: reference values. *J Neurol Neurosurg Psych* 1991;**54**:244–7.
29. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg* 1984;**9**(2):222–6.
30. Sitzia J. Volume measurement in lymphoedema treatment: examination of formulae. *Eur J Cancer Care* 1995;**4**(1):11–16.
31. Meijer RS, Rietman JS, Geertzen JHB, Bosmans C, Dijkstra PU. Validity and intra and interobserver reliability of an indirect volume determination of patients with edema of the upper extremity. *Lymphology* 2004;**37**(3):127–34.
32. van der Heijden GJ, Leffers P, Bouter LM. Shoulder disability questionnaire design and responsiveness of a functional status measure. *J Clin Epidemiol* 2000;**53**(1):29–38.
33. Kempen GI, Miedema I, Ormel J, Molenaar W. The assessment of disability with the Groningen activity restriction scale. Conceptual framework and psychometric properties. *Soc Sci Med* 1996;**43**:1601–10.
34. Suurmeijer ThPBM, Doeglas DM, Moum T, et al. The Groningen activity restriction scale for measuring disability: its utility in international comparisons. *Am J Public Health* 1994;**84**(8):170–3.
35. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European organisation for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;**85**(5):365–76.
36. Fayers P, Aaronson NK, Bjordal K, Sullivan M. *EORTC QLQ-C30 scoring manual*. Brussels: EORTC Publications; 1997.
37. Rietman JS, Dijkstra PU, Geertzen JHB, Baas P, de Vries J, Dolsma W, et al. Short-term morbidity of the upper limb after sentinel lymph node biopsy or axillary lymph node dissection for stage I or II breast cancer. *Cancer* 2003;**98**:690–6 [Erratum in *Cancer* 2004;**100**(9):1991].
38. Rietman JS, Dijkstra PU, Geertzen JHB, Baas P, de Vries J, Dolsma WV, et al. Treatment-related upper-limb morbidity one year after sentinel lymph node biopsy or axillary lymph node dissection for stage I or II breast cancer. *Ann Surg Oncol* 2004;**11**:1018–24.
41. King MT. The interpretation of scores from the EORTC quality of life questionnaire QLQ-C30. *Qual Life Res* 1996;**5**:555–67.
42. Sugden EM, Rezvani M, Harrison JM, Hughes LK. Shoulder movement after the treatment of early stage breast cancer. *Clin Oncol* 1998;**10**:173–81.
43. Bentzen SM, Overgaard M, Thames HD. Fractionating sensitivity of a functional endpoint: impaired shoulder movement after post-mastectomy radiotherapy. *Int J Radiat Oncol Biol Phys* 1989;**17**: 531–7.
44. Engel J, Kerr J, Schlesinger-Raab A, Sauer H, Hölzel D. Quality of life following breast-conserving therapy or mastectomy: results of a 5-year prospective study. *Breast J* 2004;**10**(3):223–31.